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*Sub 817*

targeting moiety:target analyte conjugate wherein the formation of the targeting moiety:target analyte conjugate decreases the clearing rate of the target analyte;

- c. obtaining a sample of blood from the human or animal after the defined period of time;
- d. combining the sample of blood with a capture moiety wherein the capture moiety binds specifically to the targeting moiety:target analyte conjugate in order to form an assay mixture;
- e. incubating the assay mixture of step d to allow the capture moiety to bind to the targeting moiety:target analyte conjugate and form targeting moiety:target analyte:capture moiety complexes in the assay mixture;
- f. removing any unbound and unconjugated targeting moiety and target analyte from the assay mixture;
- g. detecting the amount of labeled targeting moiety:target analyte:capture moiety complexes;
- h. wherein the amount of labeled targeting moiety:target analyte:capture moiety complexes detected in step (g) provides a measure of the production of secreted target analyte in the sample during the defined period of time; and
- i. wherein the target analyte is a secreted cytokine or peptide or protein hormone.

*D1 cont*

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*D2* 4. (Once Amended) The method of claim 14, wherein the target analyte is a cytokine.

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*D3* 7. (Twice Amended) The method of claim 1, wherein the blood is selected from the group consisting of whole blood, serum and plasma.

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*D4* 13. (Thrice Amended) The method of claim 1, wherein the targeting moiety is labeled with a small molecule hapten and wherein the method further comprises the step of binding the small molecule hapten to a binding partner which is conjugated to an enzyme.

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*D5* 14. (Once Amended) The method of claim 1, wherein the defined period of time is from about 1 hour to about 72 hours.

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15. (Once Amended) The method of claim 13, wherein the hapten is biotin.

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20. (Twice Amended) The method of claim 8, further comprising after step (a) the step of injecting the human or animal with an amount of second targeting moiety, wherein the second targeting moiety binds specifically to the first targeting moiety, wherein the second targeting moiety is injected in sufficient quantity that a measurable fraction of first targeting moiety is bound by the second targeting moiety and wherein the second targeting moiety is specifically bound by the capture moiety.

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25. (Once Amended) The method of claim 20, wherein the means for detecting the targeting moiety:target analyte:capture moiety complexes is by radioimmunoassay.

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26. (Twice Amended) The method of claim 20, wherein the second targeting moiety is detectably labeled by an enzymatic label.

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31. (Once Amended) The method of claim 20, wherein the capture moiety is labeled by linking to a fluorescent labeling compound.

34. (Once Amended) A reagent kit useful in performing the method of claim 1, comprising

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- (a) a first reagent comprising a labeled targeting moiety specific for the target analyte wherein the label is an enzyme indicating means operatively linked to the targeting moiety;
  - (b) a second reagent separated from said first reagent, wherein the second reagent comprises a capture moiety specific for the target analyte even when such target analyte is conjugated with the labeled targeting moiety; and
  - (c) a third reagent separated from said first and second reagents which contains a standard for the analyte.

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37. (Twice Amended) A reagent kit useful in performing the method of claim 20, comprising: (a) a first container having first targeting moieties comprising paratopic molecules that immunoreact with a target analyte, and are operatively linked to a label; (b) a second container having second targeting moieties comprising paratopic molecules that immunoreact with the target analyte at a site different from the first targeting moieties but are not in the first container; (c) a second reagent separated from said first reagent, wherein the second reagent comprises a capture moiety specific for the target analyte even when such target analyte is conjugated with the labeled targeting moiety; and (d) one or more other containers comprising one or

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more of the following: a sample reservoir, a solid phase support, wash reagents,  
reagents for detecting the presence of the first targeting moieties from the second  
container, or reagents for amplifying the label.

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Attached hereto is a marked-up version of the changes made to the specification and claims  
by this current amendment. This page is located at the end of this response and is captioned  
**"Version with Markings to Show Changes Made."**